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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,599	01/18/2005	Dominik Meyer	LUS-15874	2772

40854 7590 02/18/2009

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EXAMINER	
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ART UNIT	PAPER NUMBER
1616	
MAIL DATE	DELIVERY MODE
02/18/2009	PAPER

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/521,599
Filing Date: January 18, 2005
Appellant(s): MEYER, DOMINIK

Randolph E. Digges, III
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 11/20/08 appealing from the Office action mailed 4/18/08.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is deficient. 37 CFR 41.37(c)(1)(v) requires the summary of claimed subject matter to include: (1) a concise explanation of the subject matter defined in each of the independent claims involved in the appeal, referring to the specification by page and line number, and to the drawing, if any, by reference characters and (2) for each independent claim involved in the appeal and for each dependent claim argued separately, every means plus function and step plus function as permitted by 35 U.S.C. 112, sixth paragraph, must be identified and the structure, material, or acts described in the specification as corresponding to each claimed function must be set forth with reference to the specification by page and line number, and to the drawing, if any, by

reference characters. The brief is deficient because claim 43 is presented as an independent claim but the status of claim 43 was cancelled in the last entered claim set filed on 1/7/08.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows: there is a 35 USC 112 second paragraph rejection over claim 44. There is a provisional non-statutory double patenting rejection of claims 1, 2, and 40-42 over claims 50 and 51 of copending application 11/722779 and there is a provisional non-statutory double patenting rejection of claims 1, 2 and 40-42 over claims 39-42 of copending application 11/722857 and there is a provisional non-statutory double patenting rejection of claims 1, 2 and 40-42 over claims 94-96 of copending Application No. 11/722484.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

6261547	Bawa	7-2001
4657764	Alverez	4-1987
3368937	Macek	2-1966
6248345	Goldenheim	6-2001
3917830	Davis	11-1975
4296104	Herschler	10-1981
5061485	Oakes	10-1991
5002761	Meuller	3-1991

5942241	Chasin	8-1999
5242683	Klaveness	9-1993

Milligan et al. Anaesthesia 1988, 43, 563-564.

Strichartz. Regional Anesthesia and Pain Medicine 1998, 23(1), 3-6.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 44 recites the limitation "the mixture" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3-9 and 11-17, 26, 40-42, 44 and 45 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over Milligan et al. (Anaesthesia 1988, 43, 563-564) in view of Bawa et al. (US 6,261,547) and Goldenheim et al. (US 6,248,345) and Arias-Alvarez (US 4,657,764) and Strichartz (Regional Anesthesia and Pain Medicine 1998, 23(1), 3-6).

Applicant claims a method of treating joint pain comprising providing a neurotoxic substance dissolved in a biocompatible solvent and injecting the neurotoxic substance into a joint space such that neurolysis entails and wherein the local anesthetic is used jointly with a pH lowering additive.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Milligan et al. teach intra-articular bupivacaine for pain relief after arthroscopic surgery of the knee joint (title). Milligan et al. teach administering, by injection, sterile 20 mL solutions of 0.25% and 0.5% bupivacaine, which the Examiner interprets to mean that the "neurotoxic substance" was dissolved in a biocompatible solvent for injection (page 563, right column, middle paragraph). Since Applicant claims bupivacaine then it must be predominantly toxic to nociceptive nerve fibers but not systemically toxic and less neurotoxic to motor and propioceptive nerve fibers than to sensitive nerve fibers. It is the Examiner's position that "intra-articular" encompasses the intra-capsular region or into the joint synovial pouch.

Bawa et al. teach the equivalence of bupivacaine and levobupivacaine in anesthetic compositions (claims 6 and 7).

Goldenheim et al. teach prolonged anesthesia in joints and body spaces and methods of treating localized pain comprising administering into an intra-articular joint a formulation comprising a local anesthetic such as bupivacaine, ropivacaine, dibucaine, etidocaine, tetracaine, lidocaine, xylocaine, procaine, chloroprocaine, prilocaine, mepivacaine and mixtures thereof thus establishing equivalency among these anesthetics (Claims 1-36). Goldenheim et al. teach adding a second active agent such as an enzyme, an anti-infective agent, an antibody, a diagnostic aid, a radio-opaque dye, a magnetic resonance imaging dye, a radiolabeled agent and mixtures thereof (Claims 15, 16, 18, and 22 for example).

Arias-Alvarez teaches the use of sodium bisulfite to treat symptoms of arthritis and arthritic conditions in humans (Abstract). Aqueous solutions of from about 1 to 15% by weight sodium bisulfite are prepared for oral consumption (column 3, lines 33-35).

Strichartz teaches that high concentrations of lidocaine can be irreversibly toxic to nerves and that 5% lidocaine was shown to be neurolytic (page 3, paragraphs 2 and 3). Strichartz describes lidocaine as a neurolytic agent and teaches the *concept* of neurolysis with commonly used local anesthetics (page 4, paragraph 2 and page 5, paragraph 1).

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

1. While Applicant claims injecting the agent comprising a neurotoxic substance (local anesthetic) for treating post-operative joint pain at a concentration entailing neurolysis, Milligan

et al. do not expressly teach a method of injecting the agent comprising a neurotoxic substance (local anesthetic) for treating joint pain at a concentration entailing neurolysis. This deficiency in Milligan et al. is cured by the teachings of Strichartz, Bawa et al. and Goldenheim et al.

2. While Applicant claims using the local anesthetic jointly with a pH lowering additive ($NAHSO_3$), Milligan et al. do not expressly teach a method of wherein the local anesthetic is used jointly with a pH lowering additive that is a bisulfite (NaHSO3) in a concentration of at least 1% by weight. This deficiency is cured by the reference of Arias-Alvarez which teaches bisulfite for the treatment of the symptoms of arthritis (pain).

3. While Applicant claims a method wherein the local anesthetic is lidocaine, prilocaine, mepivacaine, levobupivacaine, ropivacaine, etidocaine, procaine, chloroprocaine, Milligan et al. do not expressly teach a method wherein the local anesthetic is lidocaine, prilocaine, mepivacaine, levobupivacaine, ropivacaine, etidocaine, procaine or chloroprocaine,. This deficiency is cured by the teachings of Bawa et al. and Goldenheim et al., which teach the equivalency of the local anesthetics to one of ordinary skill in the art.

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

1. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to inject the agent for treating joint pain at a concentration entailing neurolysis**,** in the method of Milligan et al., and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Milligan et al. teach that a concentration of 0.5% bupivacaine provided little analgesia and suggests the use

of higher concentrations of bupivacaine (Page 564, discussion). Strichartz teaches that it is known that 5% lidocaine is neurolytic. Increasing the dosage to greater than 6% results in the same outcome and is obvious to one of ordinary skill in the art of anesthesia. It is then merely routine optimization to determine the neurolytic dosage amounts of the other amide local anesthetics to be comparable to the neurolytic amount of lidocaine. In addition it would be obvious to one of ordinary skill in the art of anesthesia to add another analgesic/anesthetic to assist with producing analgesia/anesthesia and provide enhanced patient comfort. The duration of 14 days is merely routine optimization of the combination of anesthetics.

2. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to inject the agent (local anesthetic) for treating joint pain at a concentration entailing neurolysis wherein the local anesthetic is used jointly with a pH lowering additive that is a bisulfite ($NaHSO_3$) in a concentration of at least 1% by weight, as suggested by Arias-Alvarez, in the method of Milligan et al. and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because the art teaches the use of sodium bisulfite in the treatment of arthritis where the symptoms include pain (Arias-Alvarez column 1, lines 42-56). Since the same compound in the same amount for the same purpose is taught in the art as instantly claimed then it would intrinsically lower the pH of the agent for treating joint pain to less than 3.5. The claim language of instant claim 5 recites "jointly" which does not preclude oral administration of the bisulfite.

3. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use the amide anesthetics, as taught by Bawa et al. and Goldenheim et al.,

in pure enantiomeric form in the method of Milligan et al. in the amount claimed and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Milligan et al. suggest using higher dosages of the anesthetic and the art teaches the equivalence of the amide anesthetics. Since the art teaches the equivalence of the amide anesthetics and it is merely judicious selection to pick the proper amide and routine optimization to arrive at the proper concentration especially when the art, Milligan et al., teaches higher dosages. Therefore, it is the Examiner's position that a concentration of local anesthetic > 4%; lidocaine > 6%; prilocaine > 3%; mepivacaine > 5%; bupivacaine > 1.5%; levobupivacaine > 5%; ropivacaine > 2%; etidocaine > 2%; procaine > 3%; chloroprocaine are all reasonably within routine optimization of the method of Milligan et al. by one of ordinary skill in the art. It is common sense that one of ordinary skill in the art would want the highest purity pharmaceutical agents in the preparation and that would encompass the enantiomeric forms as well.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976).

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at

the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claim Rejections - 35 USC § 103

Claims 1, 3-8, 11, 13, 26, 28, 35 and 40-42 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over Macek et al. (US 3,368,937).

Applicant claims a method of treating joint pain comprising providing a neurotoxic substance dissolved in a biocompatible solvent and injecting the neurotoxic substance into a joint space such that neurolysis entails and wherein the local anesthetic is used jointly with a pH lowering additive.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Macek et al. teach an injectable steroid anesthetic composition and teach administering a combined dosage of steroid and an aromatic amide (lidocaine and mepivacaine) (Column 1, lines 55-72). The route of administration can be intramuscular, intrasynovial, intra-ocular and soft tissue injection (column 1, lines 17-20). Macek et al. teach compositions comprising lidocaine, dissolved in water, dexamethasone, sodium bisulfite, phenol and water to create a water-soluble product (column 3, example 1, lines 22-40). Phenol is present as a bacteriological preservative

(column 3, line 37 and claim 11, for example). The injectable solution consists essentially of a biocompatible solvent, water, **about 5-20 parts by weight of lidocaine or mepivacaine** and about 1-20 parts by weight of the steroid with water to 1 ml (Claims 1, 11 and 12). In the absence of evidence to the contray, the anesthetics used by Macek et al. are in their pure enantiomeric form. Since Applicant claims lidocaine then it must be predominantly toxic to nociceptive nerve fibers but not systemically toxic and less neurotoxic to motor and propioceptive nerve fibers than to sensitive nerve fibers.

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

1. While Applicant claims a method of treating *post-operative joint pain* comprising providing a neurotoxic substance dissolved in a biocompatible solvent and injecting the neurotoxic substance into a joint space such that neurolysis entails, Macek et al. do not expressly teach a method for treating *post-operative joint pain* comprising injecting an agent comprising a neurotoxic substance (local anesthetic) at a concentration entailing neurolysis. However, Macek teach such conditions as rheumatoid arthritis, bursitis and sprains *and the like* but does not specifically mention post-operative pain (column 1, lines 20-23).

2. While Applicant claims a method wherein the nociceptive nerve fibers are rendered pain-insensitive by the local anesthetic or the mixture of several local anesthetics for at least 14 days, Macek et al. do not expressly teach the duration of action of the injectable solution.

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

1. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to treat post-operative pain with the composition and method of Macek et al. and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Macek et al. describe several types of painful joint trauma and suggests others ("and the like") such that one of ordinary skill in the art would immediately envision alleviation of joint pain associated with an operation.

2. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to treat post-operative pain with the composition and method of Macek et al. wherein the nociceptive nerve fibers are rendered pain-insensitive by the local anesthetic or the mixture of several local anesthetics for at least 14 days and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Macek et al. teach using up to 20 parts by weight of the anesthetic (claim 1) which encompasses that which is instantly claimed and would therefore have the same duration of action.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976).

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claim Rejections - 35 USC § 103

Claims 1, 5, 28-37, 39 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Macek et al. (US 3,368,937) in view of Goldenheim et al. (US 6,248,345) and Strichartz (Regional Anesthesia and Pain Medicine 1998, 23(1), 3-6) and with respect to claims 34 and 37 Davis et al. (US 3,917,830) and with respect to claim 39 Herschler (US 4,296,104) and with respect to claims 28-30 Oakes et al. (US 5,061,485) and with respect to claims 31 and 32 Meuller (5,002,761) and with respect to claim 36 Chasin et al. (US 5,942,241) and with respect to claim 33 Klaveness (US 5,242,683).

Applicant claims a method of treating joint pain comprising providing a neurotoxic substance dissolved in a biocompatible solvent and injecting the neurotoxic substance into a joint space such that neurolysis entails and wherein the local anesthetic is used jointly with a pH lowering additive and in addition to the local anesthetic: 1) cresol; 2) a chloro cresol; 3) eugenol; 4) thymol; 5) x-ray contrast reagent; 6) glycerin; 7) vasoconstrictor; 8) DMSO, and 9) polyethylene glycol are added.

Determination of the scope and content of the prior art

(MPEP 2141.01)

The references of Macek et al., Strichartz and Goldenheim et al. are discussed in detail above and those discussions are hereby incorporated by reference.

Oakes et al. teach the equivalence of phenol, cresol , m-, o-, p-chlorocresol etc… as germicidal agents (column 5, lines 60-68 and claim 29 for example).

Herschler teaches DMSO as a known penetration enhancer for pharmaceutical agents such as analgesics, steroids and anti-inflammatory agents (column 4, lines 41-47).

Davis et al. teach an injectable steroidal anesthetic wherein the injection medium comprises propylene glycol, glycerol or glycerol formal of greater than 50% of the total injection and teaches polyethylene glycols (claims 1-4 and column 7, lines 3-7).

Mueller et al. teach the equivalence of thymol and eugenol as preservatives (column 4, lines 11-16 and claim 18).

Chasin et al. teach formulations and methods for providing prolonged local anesthesia comprising vasoconstricting agents such as epinephrine (which is synonymous with adrenaline), norepinephrine and phenylphrine and local anesthetics such as bupivacaine (Abstract, column 9, lines 60-65; claims 1-8, 11, 12 and 23-33, for example).

Klaveness teaches contrast media comprising a paramagnetic agent and an iodinated agent for X-ray and MRI (Title; abstract). Barium and iodine are taught as contrast agents (column 1, lines 15-18). The paragmagnetic metal can be gadolinium (Claims 1 and 9).

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

1. While Applicant claims a method of treating post-operative joint pain comprising providing a neurotoxic substance dissolved in a biocompatible solvent and injecting the neurotoxic substance into a joint space such that neurolysis entails and wherein the local anesthetic is used jointly with a pH lowering additive and in addition to the local anesthetic: 1) cresol; 2) a chloro cresol; 3) eugenol; 4) thymol; 5) x-ray contrast reagent; 6) glycerin; 7) vasoconstrictor; and 8) DMSO, are added, Macek et al. do not expressly teach the addition of these components in a method of treating post-operative joint pain but as explained above, Macek et al. suggest treating pain in joints which would include post-operative joint pain.

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

1. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to add 1) cresol; 2) a chloro cresol; 3) eugenol; 4) thymol; 5) x-ray contrast reagent; 6) glycerin; 7) vasoconstrictor; and 8) DMSO**,** as suggested by Oakes, Herschler, Davis, Mueller, Chasin and Klaveness, to the method of Macek et al. and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because: 1 and 2) Macek et al. teach phenol as a preseservative which renders other phenols, such as those taught by Oakes et al. obvious to one of ordinary skill in the art; 3 and 4) eugenol and thymol are also taught as preservatives by Meuller et al. and are phenols and would be obvious to one of ordinary skill in the art; 5) Goldenheim teaches the addition of diagnostic agents to intra-articular joint a formulations comprising a local anesthetic but does not specifically name them and Klaveness

cures that deficiency by teaching the types of X-ray contrast reagents known to one of ordinary skill in the art; 6) Davis teaches glycerol as a medium for injection of these solutions which is known to one of ordinary skill in the art; 7) Chasin teach that addition of vasoconstrictive agents might greatly prolong local anesthetic activity (column 9, lines 4-25); and 8) Herschler teaches DMSO as a known penetration enhancer. It is the Examiner's position that with the exception of the vasoconstrictor the other additional components are readily known to one of ordinary skill in the art. The motivation to add the vasoconstrictor comes from the teaching that it can provide prolonged anesthetic activity. Strichartz is cited for the teaching that it is known to one of ordinary skill in the art that high concentrations of local anesthetics are neurolytic and entail neurolyis.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976).

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).s

1. Claims 1, 2 and 40-42 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 50 and 51 of copending Application No. 11/722,779. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed subject matter is embraced by or embraces the subject matter of the co-pending application. Instant claim 1 is drawn to a method of treating joint pain comprising providing a neurotoxic substance dissolved in a biocompatible solvent and injecting the neurotoxic substance into a joint space such that neurolysis entails. Copending claim 50 is drawn to a method of treatment of pain with resiniferatoxin dissolved in a solvent compatible with the body in a volume of 0.1 to 150 mL and injected into the intracapsular region such that neurolysis occurs. Instant claim 42 recites a period of 14 days and copending claim 51 recites at least 14 days. One of ordinary skill in the art would have recognized the obvious overlap in subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

2. Claims 1, 2 and 40-42 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 39-42 of copending Application No. 11/722,857. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed subject matter is embraced by or embraces the subject matter of the co-pending application. Instant claim 1 is drawn to a method of treating joint pain comprising providing a neurotoxic substance dissolved in a biocompatible solvent and injecting the neurotoxic substance into a joint space such that neurolysis entails. Copending claims 39, 40, 41 and 42 recite a method for the treatment of articular pain wherein an agent is injected into the intracapsular region of a joint affected by pain; wherein the agent is dissolved in a solvent compatible with the body and 0.1 to 150 ml of the solution is injected into intracapsular region; nociceptive fibers are made insensitive to pain for at least 14 days; and neurolysis occurs. One of ordinary skill in the art would have recognized the obvious overlap in subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

3. Claims 1, 2 and 40-42 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 94-96 of copending Application No. 11/722,484. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed subject matter is embraced by or embraces the subject matter of the co-pending application. Instant claim 1 is drawn to a

method of treating joint pain comprising providing a neurotoxic substance dissolved in a biocompatible solvent and injecting the neurotoxic substance into a joint space such that neurolysis entails. Copending claims 94-96 recite a method for the treatment of joint pain wherein an agent is injected into the intracapsular region or into the joint capsule of a joint affected by pain; wherein the agent is dissolved in a solvent compatible with the body and 0.1 to 150 ml of the solution is injected into intracapsular region or into the joint capsule of a joint affected by pain; nociceptive fibers are made insensitive to pain for at least 14 days; and neurolysis occurs. One of ordinary skill in the art would have recognized the obvious overlap in subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

(10) Response to Argument

With regards to the rejection of claims 1, 3-9 and 11-17, 26, 40-42, 44 and 45 under 35 U.S.C. 103(a) as being unpatentable over Milligan et al. (Anaesthesia 1988, 43, 563-564) in view of Bawa et al. (US 6,261,547) and Goldenheim et al. (US 6,248,345) and Arias-Alvarez (US 4,657,764) and Strichartz (Regional Anesthesia and Pain Medicine 1998, 23(1), 3-6), Appellant asserts that the reference of Milligan suggests the source of the pain was likely outside the capsule of the knee joint and therefore one of ordinary skill in the art would not be motivated to inject higher concentrations into the post-operative joint. However, it is mere speculation on the source of the pain and speculation cannot substitute for definitive objective support. The pain could just as well be in the capsule of the knee joint. **The fact** remains that Milligan suggests the

use of higher concentrations of bupivacaine (Page 564, discussion). Appellant asserts that: ""Strichartz questions whether a neurolytic mechanism can explain the three cases reported in the Choi et al. case report, none of which involved injections into a post-operative joint space. This clearly contradicts the Examiner's contention that the "concept of high concentrations of local anesthetics being neurolytic is known in the art and not anything new."" This is factually incorrect and the line of reasoning is not persuasive. **The fact** is that Strichartz is relied upon for teaching, for example: "It is clear, nonetheless, from the reports of cauda equina syndrome due to 5% lidocaine spinal anesthesia (2-5) and 2% lidocaine intended for epidural anesthesia (4, 5), and the resulting publications of in vitro (21-24) and in vivo (25-27) animal studies to explain this devastating injury, **that high concentrations of lidocaine can be irreversibly toxic to nerves**." And; "There are potential advantages to **using lidocaine as a neurolytic agent in lieu of the currently used drugs**." (Examiner added emphasis: See page 3, second paragraph through page 4, third paragraph). ***Cleary the art recognizes lidocaine as a neurolytic agent as asserted by the Examiner!***

Appellant's assertion that the secondary references are inapposite thus implying analogous art is not compelling. MPEP 2141.03 states (in part), "**A person of ordinary skill in the art is also a person of ordinary creativity, not an automaton**." *KSR International Co. v. Teleflex Inc., 127 S.Ct. 1727, 167 LEd2d 705, 82 USPQ2d 1385, 1397 (2007)*. "[I]n many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle." *Id*. (Examiner added emphasis).

Appellant's separate argument for claims 6 and 7 is not persuasive. The art teaches using bisulfite for treatment of arthritis and arthritic conditions which is directed to the same field as

Milligan which joint disorders (arthroscopy). No unexpected results have been shown for adding bisulfite.

Appellant's separate argument for claims 11-17 is that no reference of record teaches or suggests a solution for injection into a post-operative joint space at the instantly claimed concentrations. It is correct that no anticipatory art has been applied against the instantly claimed subject matter. However, in the analysis for obviousness, it is the Examiner's position that at least 5% lidocaine is known to be neurolytic and therefore any amount greater than 5% lidocaine is also neurolytic. *This concept is established in the art.* Again, Appellant attempt to distract from the facts of the case by focusing on the ophthalmic solutions of Goldenheim. Goldenheim teaches the fact that the instantly claimed amide anesthetics are known in the art and are functional equivalents. No unexpected results have been shown.

Summary

- Fact #1: The art teaches treatment of post-operative pain with amide anesthetics and suggests using higher concentrations.
- Fact #2: The art teaches the equivalence of amide anesthetics such as bupivacaine and lidocaine.
- Fact #3: The art teaches higher concentrations of lidocaine (5%) are neurolytic and, contrary to Appellant's assertions, the concept of high concentrations of amide anesthetics acting neurolytically is already common public knowledge.

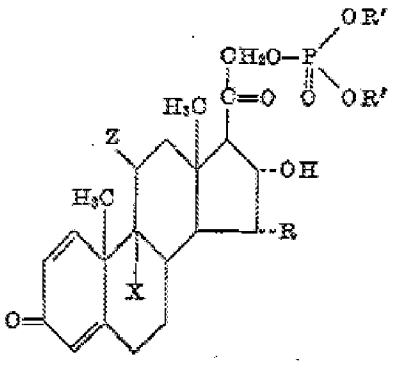
With regard to the rejection of claims 1, 3-8, 11, 13, 26, 28, 35 and 40-42 under 35 U.S.C. 103(a) as being unpatentable over Macek et al. (US 3,368,937) as well as claims 1, 5, 28-37, 39 and 46 under 35 U.S.C. 103(a) as being unpatentable over Macek et al. (US 3,368,937)

in view of Goldenheim et al. (US 6,248,345) and Strichartz (Regional Anesthesia and Pain Medicine 1998, 23(1), 3-6) and with respect to claims 34 and 37 Davis et al. (US 3,917,830) and with respect to claim 39 Herschler (US 4,296,104) and with respect to claims 28-30 Oakes et al. (US 5,061,485) and with respect to claims 31 and 32 Meuller (5,002,761) and with respect to claim 36 Chasin et al. (US 5,942,241) and with respect to claim 33 Klaveness (US 5,242,683), the cornerstone of Appellant's argument is that the claim language of Macek et al. is incorrect. On page 17 of the Appeal Brief, Appellant asserts: "However, claim 1 of Macek et al. clearly includes an error. The first word of the fourth line of claim 1 of Macek et al. is incorrectly recited as "and" when it clearly should be the word "to". Appellant appears to be attempting to amend a patented claim.

Claim 1 of Macek is reproduced below with Examiner added emphasis.

What is claimed is:

1. A clear, injectable solution consisting essentially of water, about 5–20 parts by weight of a compound selected from the group consisting of lidocaine and mepivacaine and about 1–20 parts by weight of a compound represented as:



wherein X is selected from the group consisting of hydrogen and fluorine, Z is selected from the group consisting of keto and hydroxy, R is selected from the group consisting of hydrogen and methyl and R^1 is selected from the group consisting of hydrogen and sodium.

The claim language is clear and definite and the Examiner can find no fault in the subject matter of claim 1 of Macek. Appellant's argument that various embodiments of Macek contain amounts of active that are below the instantly claimed amounts and therefore claim 1 of Macek is limited to that scope is not persuasive and is in error. The scope of the teachings of Macek is not limited to these embodiments. Since Appellant's argument to remove Macek as art is not persuasive then Appellant's other arguments fall as well and the rejections stand.

With regards to the rejection of claim 44 under 35 USC 112 second paragraph, Appellant reserves the right to file an amendment to amend claim 44 subsequent to a Decision on this appeal.

With regards to the provisional double patenting rejections, Appellant reserves the right to file terminal disclaimers to obviate the rejections subsequent to a Decision on this appeal.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Johann R. Richter/

Supervisory Patent Examiner, Art Unit 1616

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/Ernst V Arnold/

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